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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,825	09/22/2000	Satoshi Mori	55022	1169

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,825	MORI ET AL.	
	Examiner	Art Unit	
	Mary M. Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/2002, has been entered.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 since the brief description of the drawings does not refer to the nucleic acids in the figures by SEQ ID NO. (See pages 6-7) Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. Applicant's response to the instant Office action will be held non-responsive if the response does not place the specification in compliance with the sequence rules.

Drawings

3. The drawings dated 9/22/2000, are objected to because of the informalities noted in the PTO-948 attached to the Office action mailed 05/22/2002. A proposed drawing correction or

corrected drawings are required in reply to the Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

4.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 33, 36, 37, 38, 41, 44 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 and 41 are indefinite for the language "such that G+C content is consistent throughout the entire sequence" since the metes and bounds of what G+C levels are considered "consistent" is not defined in the specification as filed. Claims 36-39, 44 and 45 are rejected for their dependency on claim 33 or 41. The specification as filed teaches on page 5, lines 10-12, for instance that "[i]n the method of the present invention, it is preferable that base G and T rich region in the gene to be introduced is small; difference in content of base G and C within whole region of the gene to be introduced is small...." However, from such description, it is not clear how the introduction of "small" amounts of G and C into the gene correlates to a "consistent" presence of G+C in the entire gene. Every gene differs naturally in their amount of G+C, and

thus the amount to be "consistent", or the particular placement of the G+C in certain places in the gene is not clear from the specification as filed.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 30-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 30 is drawn to nucleic acids having a modified base sequence of a gene for transforming a plant, wherein the sequence is modified by features (A) and (B) without altering the amino acid sequence, for eliminating the sequences relating to poly(A) addition, wherein features (A) and (B) are defined as follows:

(A) GT rich regions comprising 8 or more consecutive bases of G or T are eliminated, and

(B) sequences encoded by AATAAA, NATAAA, ANTAAA, AANAAA, AATNAA, AATANA, or AATAAN are eliminated.

Claims 31, and 39-44 specify that the gene is from yeast, but does not further specify a particular yeast gene or set of genes. Claim 37 specifies that gene encodes ferric-chelate

reductase FRE1, but does not specify from what organism. Claims 39-44 specify that the nucleic acid sequence is a modified yeast ferric-chelate reductase gene, but does not further specify the sequence of any yeast ferric-chelate reductase gene(s) other than instant SEQ ID NO:1.

Claims 32-38 and 40-43 are included in the instant rejection for their dependency on rejected claims 30 and 39.

Claims 33, 36-38, 41 and 44-45 are further included in the instant rejection for the content of claims 33 and 41 (rejected under 35 U.S.C. 112, 2nd paragraph, above).

The specification as filed teaches the novel modified FRE1 sequence of SEQ ID NO:1 from *Saccharomyces cerevisiae*. The modified FRE1 was shown to have ferric-chelate reductase activity as shown in instant Figures 16 and 17.

The instant claims are drawn to any modified nucleic acid sequence as reiterated above. The specification describes on page 5 that an "[e]xample of the region of a factor relating to the poly(A) addition of the mRNA is preferably AATAAA like base sequence, further the said region of a factor relating to the poly(A) addition of the mRNA is preferably the region existing downstream of the GT-rich base sequence." The specification teaches by way of example modification of the yeast FRE1 gene since the full length mRNA of yeast FRE1 introduced into tobacco plants was not able to be expressed due to "addition of poly (A) within the coding region of FRE1." (See page 10 of the specification)

It was not clear at the time the invention was made that Applicant was in possession of a representative number of species of any modified nucleic acid sequence as broadly claimed. The breath of any nucleic acid claimed rests on negative limitations so that Applicants' claim any nucleic acid sequence which potentially has the omission of certain GT rich regions and sequences encoded by an AATAAA region, NATAAA, ANTAAA, AANAAA, AATNAA, AATANA, or AATAAN. The specification as filed doesn't provide any other example genes which would require such modification other that the yeast FRE1 gene for expression in tobacco. Therefore, other than a vague teaching to look for GT-rich areas in any such gene, and change the sequence to remove certain sequences, one of skill in the art would not immediately envision what is otherwise any possible nucleic acid gene sequence as broadly claimed. The art indicates that the structure of nucleic acid sequences, ie. any gene for instance, is empirically determined and the structural elements of a gene in one species will have different regulatory sequences and different structural elements. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO:1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims.

Furthermore, MPEP 608.01(p) states that ""Essential material" is defined as that which is necessary to (1) describe the claimed invention..." and such essential material may not be incorporated by reference into the instant specification as filed. It would be essential to know other starting gene sequences which would be applicable to the instantly claimed modifications in order to show that applicant was in possession of a representative number of species of such template sequences at the time the invention was made.

Finally, in view of the 35 U.S.C. 112, 2nd paragraph, rejection above, applicant is not considered to have adequately described a representative number of species of any gene sequence as claimed in claims 30 and 39, wherein "the base sequence is optimized such that G+C content is consistent throughout the entire sequence..." since neither the specification nor the prior art taught an art recognized definition for what a "consistent" amount of G+C content looks like in a gene sequence. The art recognizes that G+C content is found in a certain percentage in a gene sequence, but does not further specify the amount, nor the placement of the G and C sequences that is considered "consistent" for any possible gene sequence. As such, applicant has not clearly described the claimed invention such that one of skill in the art would have recognized that applicant was in possession of a representative number of species of any gene sequence having the optimized consistent use of G+C content since no standard level or placement of G+C content is defined in the specification as filed or the prior art.

One of skill in the art was in possession of the sequence of SEQ ID NO1, the modified nucleic acid sequence of *Saccharomyces cerevisiae* FRE1 gene.

Response to Arguments

Applicant's arguments filed 10/01/2002 have been fully considered but they are not persuasive.

On page 5 of the response, applicant states that "Attention is directed to the present application at page 3, line 22, to page 4, line 12, where Applicants describe certain instances where in complete transcription has been achieved, e.g., where a gene of another species has been transformed into a higher plant by introducing a gene of another organism species. It is noted the although transformation of the higher plant has been shown, expression was low to non-existent."

The specification taught on page 3, line 22, to page 4, line 12, that the gene group Cry are insecticidal proteins that would be useful targets for the instantly claimed modifications. However, this family of gene sequences is not specifically claimed in the instant claims, and is not considered representative for the entire genus of any possible gene claimed, or any possible yeast gene, for administration to plants.

Applicant further states on page 5 of the response that "The present invention provides novel methodology for gene modification to improve the expression of a foreign gene. The underlying principle of Applicants' invention is based on the difference among the transcriptional system of the plant and that of the donor species. It is respectfully submitted that a person skilled in the art could readily apply Applicants' novel methodology for introducing any foreign gene

into any plant species. In that way, Applicants' disclosure (together with the level of knowledge and skill in the art) is enabling well beyond the case where the yeast FRE1 gene is introduced into tobacco...."

In response, since applicant rebutted both 35 U.S.C. 112, first paragraph, rejections made in the previous Office action, simultaneously, it appears that applicant is rebutting the scope of enablement rejection with the above comment. Nevertheless, the comments are not considered persuasive for overcoming the above 35 U.S.C. 112, first paragraph, lack of written description rejection since the instant claims are not drawn to methods of making the instant nucleic acid constructs, but rather, are drawn to the actual compositions produced. As such, regardless of how the claimed compositions are made, applicant is not considered in possession of a representative number of species of the claimed nucleic acids for the reasons set forth above.

Applicant further states on page 6 of the response that "Applicants surprisingly discovered that the GT rich region located upstream of the polyadenylation signal sequence (AATAAA like sequence) defines the addition of poly(A) of mRNA (polyadenylation)...."

However, this discovery by applicant is not considered to further place applicant in possession of the claimed breath of nucleic acids since the claims are not drawn to methods of identification of poly(A) addition sites having upstream GT rich regions, but are rather drawn to compositions of nucleic acids, the breath of which is not considered adequately described for the reasons set forth above.

The remainder of applicants remarks on pages 6-8 of the response filed 10/01/2002 are drawn to enablement the claimed invention and do not pertain to the above 35 U.S.C. 112, lack of written description, rejection.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 30, 32, 33, 36 are rejected under 35 U.S.C. 102(a) as being anticipated by Wilson et al. (Biochemical and Biophysical Research Communications, Vol. 232, pp. 678-681, 1997).

Claim 30 is drawn to a nucleic acid having a modified base sequence of a gene for transforming a plant, wherein the sequence is modified by features (A) and (B) without altering the amino acid sequence, for eliminating the sequences relating to poly(A) addition, wherein features (A) and (B) are defined as follows:

(A) GT rich regions comprising 8 or more consecutive bases of G or T are eliminated and

(B) sequences encoded by AATAAA, NATAAA, ANTAAA, AANAAA, AATNAA, AATANA, or AATAAN are eliminated.

Wilson et al. teach on page 679, in Figure 1, the nucleic acid sequence of *Arabidopsis thaliana* Ins (1,3,4)P_3 5/6-kinase gene which meets all the structural limitations of instant claim 30 since it is a sequence the does not contain either feature (A), any GT rich region comprising 8 or more consecutive bases of G or T, nor feature (B), sequences encoded by AATAAA. Although the Wilson et al. sequence has in positions 962-968, the sequence "AAATAAA", this sequence is not found within the coding region of the gene (it is part of the 3' UTR). Furthermore, this apparently is not a poly(A) addition region since the reference teaches on page 679, col. B, lines 10-12, that "[t]here is no polyadenylation signal or poly (A) tail, suggesting that part of the 3' end is not contained within this clone. Since this nucleic acid sequence was found to encode a functional Ins (1,3,4)P_3 5/6-kinase protein (see page 680, col. 1, lines 8-12), the Ins (1,3,4)P_3 5/6-kinase gene sequence is considered to read on the instantly claimed gene sequence.

Claim 32 further claims the nucleic acid according to claim 30, wherein codon usage of the base sequence is modified to increase a preferred codon of the plant.

Since the Ins (1,3,4)P_3 5/6-kinase gene sequence taught by Wilson et al. was an *Arabidopsis* sequence, this limitation is inherently met, since the Wilson et al. sequence already has plant gene codon usage.

Claim 33 further claims the nucleic acid according to claim 30, wherein the base sequence is optimized such that G+C content is consistent throughout the entire sequence, without altering the amino acid sequence.

The Ins (1,3,4)P_3 5/6-kinase gene has a G+C content that is considered to meat the limitations of the claim since the structural features of the limitation "consistent" are not further defined by the instant specification as filed (see the 35 U.S.C. 112, 2nd paragraph, rejection above).

Claim 36 is drawn to the nucleic acid according to claims 30-35, wherein the nucleic acid is DNA.

The Ins (1,3,4)P_3 5/6-kinase nucleic acid sequence taught by Wilson et al. in Figure 1 is a DNA coding sequence.

10. Claims 31, 34, 35 and 37-45 are considered free of the prior art for the following reasons: Claims 38 and 45 are free of the prior art since the prior art did not teach nor fairly suggest the nucleic acid sequence of instant SEQ ID NO:1; The prior art did not teach nor fairly suggest a yeast sequence without a poly(A) signal region (an AATAAA, NATAAA, AANAAA, AATNAA, AATANA, or AATAAN), or further, without a Kozak sequence (a feature of eukaryotic genes). The prior art did not teach nor fairly suggest a sequence meeting the

limitations of instant claim 30, and also missing all "ATTA" sequences (The Ins (1,3,4)P_3 5/6-kinase nucleic acid sequence taught by Wilson et al. has an ATTA sequence).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Inquiries relating to the status of this application may also be directed to *Katrina Turner*, whose telephone number is (703) 305-3413.

SEAN McGARRY
PRIMARY EXAMINER

M. M. Schmidt
February 6, 2003